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Three fellows have been selected from 20 applicants plus five internal candidates. They are: Scott Jepson working on "P53 Function and Regulation of Telomerase Activity in Human Epithelial Cells", Anna Erickson on "Radiation Regulation of E-Cadherin" and Rana Zahedi on "Identification of the Protease that Regulates the Morphogenic Effects of the Mammary Morphogen, Epimorphin". The candidates are expected to spend at least 90% of their time at the bench. In addition, they attend weekly group meetings of the PIs as well as weekly seminars, forums, and mammary affinity groups. Each candidate works with two faculty.

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## **DOD Training Grant in Mammary Biology 2001 Annual Report**

### **Introduction**

The goal of the present proposal is to provide post-doctoral training opportunities in breast cancer research that focus on the role of microenvironment in mammary gland biology. Trainees will benefit from working in a dynamic interactive program under the guidance of the LBNL mentors to investigate the intersection of hormone action, growth factor activity and extracellular matrix remodeling during mammary gland development and carcinogenesis. In addition, trainees will be exposed to a variety of other topics related to breast cancer, as well as research ranging from molecular medicine to genomics, by their participation in working groups, lectures and scientific meetings with other Berkeley Lab and Bay Area researchers.

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### **Recruitment**

Applicants for the postdoctoral fellowships were recruited by posting advertisements at major cancer meetings, on mammary biology lists and through the Lawrence Berkeley National Laboratory Human Resources webpage. In addition, personal contacts and unsolicited applicants to individual mentors were considered for these positions.

- American Association of Cancer Research posting
- LBNL web posting: Initial #13392, Ongoing #13447; Web address: <http://cjo.lbl.gov/>
- Posted to Mammary Biology List (maintained by P. Neville at the University of Colorado)

The text of the posting was as follows:

Several postdoctoral training positions are available to study mammary biology and breast cancer using human and mouse mammary cell culture and animal models. Fellows will conduct a research project defined by collaboration of two mentors in a DOD –BCRP funded postdoctoral training program. Research areas include growth factor biology and signaling, mechanisms of differentiation, senescence and neoplastic progression, radiation biology, cell-cell and cell-extracellular matrix interactions, tumor biology, and hormone action.

Requirements: Recent Ph.D. in cell and molecular biology or related field. Ability to work with guidance of principal investigator and collaborators. Ability to conduct experiments independently, maintain appropriate records and manage data. Excellent verbal and written communication.

### **Screening and Selection**

Approximately 20 applicants responded. Their letters and CVs were circulated to the mentor groups. Mentors then indicated their enthusiasm for individual applicants, who were invited to LBNL to present their current research. Mentors interviewed applicants and discussed possible research projects. Candidates were informed at the time that their research projects would be the result of collaboration between at least two mentors. Three candidates were recruited.

### **Postdoctoral Fellows 2000-2001**

- Ana Erickson, Ph.D.

Dr. Erickson joined the Barcellos-Hoff lab in June 2001 to conduct research on a joint project with Dr. Barcellos-Hoff and Bissell. She obtained her degree in Cell Biology from the University of Alabama at Birmingham in 2001 in the laboratory of Dr. John Couchman. Her expertise in proteoglycan biology and molecular biology provides an excellent background for her current project to study the underlying molecular mechanisms controlling the expression of E-cadherin in irradiated human mammary cells. She will examine E-cadherin mRNA, protein abundance and localization, and its association with other membrane and cytoskeletal proteins in cells surviving radiation exposure in the three-dimensional model of alveolar morphogenesis.

- Rana Zahedi, Ph.D.

Dr. Zahedi joined Dr. Bissell's laboratory in 2000 as a senior Postdoctoral Fellow. She obtained her Ph.D. in Protein Chemistry/Toxicology in 1996 at the University of Paris VII, Paris, France.

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She conducted postdoctoral training from 1997-2000 at The Center for Blood Research, Harvard Medical School, Boston, Massachusetts. Her research project will identify the putative membrane bound protease necessary for cleaving epimorphin. The activated protease is postulated to cleave and release the soluble form of epimorphin, which apolar presentation to mammary epithelial cells mediates alveolar formation. She will determine the properties of the protease that cleaves epimorphin, and further purify and identify the protease to analyze the consequences of its over-expression or repression of the identified in culture and in vivo.

- **Scott Jepson, Ph.D.**

Dr. Jepson joined the laboratory of Dr. Yaswen in June 2001. He obtained his doctoral degree in Immunology with Dr. Ian Hutchinson in 1999 from the University of Manchester, Manchester, England. He conducted postdoctoral training in the laboratory of Dr. Kermit Carraway at the University of Miami School of Medicine studying MUC4 in mammary tumorigenesis. He will study p53 function during immortalization and radiation exposure of human mammary epithelial cells, identify p53 dependent pathways that influence telomerase expression, and determine whether p53 responsiveness of normal/immortal HMEC is modulated by the cytokine, TGF $\beta$ . These studies are in collaboration with Dr. Barcellos-Hoff.

### **Training Activities**

The trainees are exposed to a wide range of research approaches, tools, and methods that are encompassed in the mentor's laboratories. In addition to weekly **laboratory meetings** with the preceptor, a monthly **Cell and Molecular Biology department meeting** is held to bring together the investigators and the trainees to discuss research and literature relevant to the program. The department will host a Postdoctoral Research Day on December 5 that will feature poster presentations and a speaker chosen by postdoctoral fellows. **Division seminars** are held weekly (see Attachment 1 consisting of a roster of speakers for 2000-2002).

Of particular relevance is the monthly **Mammary Gland Affinity Group**, which is a long standing tradition. LBNL mammary biology and breast cancer groups meet for informal research presentations. Additional participants from UC San Francisco Medical Center and UC Berkeley campus attend regularly. The format depends on the speaker. Both LBNL mentors and external speakers give informal, "chalk" talks in areas of basic biology of mammary gland. Examples include: Dr. Dan Medina from Baylor College discussed preneoplastic lesions in the mouse mammary gland. Dr. Olé Petersen from Denmark discussed the characterization and culture of cellular constituents of the human mammary gland. Dr. Gilbert Smith from National Cancer Institute discussed the nature of mammary stem cells. Dr. S. Nandi discussed hormonal regulation of breast cancer progression. Currently, the format consists of two short talks by postdoctoral fellows. Approximately 30-40 participate.

The Life Sciences Division currently hosts approximately 50 research grants in breast cancer and mammary biology, totaling over \$10 million in funds. We are pleased with the recent establishment of a laboratory wide program entitled, **The Breast Cancer Research Awareness Forum**, held monthly for a general audience highlighting research at LBNL. Dr. Mina Bissell, the Principal Investigator of the Training Grant, chairs these sessions. The first forum, on August 23, 2001, was on the role of hormones in breast cancer prevention and treatment and featured Susan Love, M.D., Adjunct Professor of Surgery at the University of California, Los Angeles and Satyabrata Nandi, Ph.D., Professor of Cell and Developmental Biology, University

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of California, Berkeley. The second forum, held on September 10, 2001, featured Berkeley Lab's Mary Helen Barcellos-Hoff, Ph.D. Head of the Lawrence Berkeley National Laboratory's Life Sciences Cancer and Tissue Biology Group, and Bill Moses, Ph.D., Senior Staff Physicist in LBNL's Department of Functional Imaging. Their discussion will provide an overview of Life Sciences Division's breast cancer research activities, from molecular, cellular and radiation biology to the development of new compact and ultra sensitive imaging devices for the detection of breast cancer. David Irwin, M.D., Director of Clinical Research at the Alta Bates Comprehensive Cancer Center in Berkeley and Berkeley Lab employee Ms. Sonia Miller will present the next planned forum on Clinical Trials in October. Ms. Mueller will bring a patient's perspective to the event and will be joined by her oncologist, Dr. Irwin. In November, Debu Tripathy, Ph.D., Associate Clinical Professor of Medicine at the University of California at San Francisco, will provide the overview of research & a scientific context while Berkeley acupuncturist, Isaac Cohen, M.D., will speak on Alternative Therapies. In 2002, Mina J. Bissell, Ph.D., Director of the Life Sciences Division at Lawrence Berkeley National Laboratory will give a forum on epidemiology. Subsequent forums will investigate other emerging breast cancer surgery and treatment options. The forums are an important avenue for postdoctoral fellows to learn not only about research but also how to communicate about their research with a lay audience.

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**Reportable Outcomes**

We have succeeded in attracting three capable scientists who have been working with six of the faculty. However, because of the time that it took to accomplish this recruitment, there have been no reportable outcomes as yet.

## Attachment 1 Roster of Speakers List for 2000-2002

DATE	SPEAKER	AFFILIATION
<b>2000</b>		
19-Sep-00	Gerard I. Evan,	University of California, San Francisco
24-Oct-00	Phoebe L. Stewart	University of California, Los Angeles, School of Medicine
7-Nov-00	Cynthia Kenyon	University of California, San Francisco
16-Nov-00	John C. Schimenti	The Jackson Laboratory
28-Nov-00	Russ Altman	Stanford University Medical School
6-Dec-00	Ursula Klingmuller	Max-Planck-Institute of Immunobiology
14-Dec-00	Joachim Rychly	University of Rostock
<b>2001</b>		
9-Jan-01	Martin McMahon	University of California, San Francisco
19-Jan-01	Satyabrata Nandi	University of California, Berkeley
30-Jan-01	Gene E. Robinson	University of Illinois
6-Feb-01	Ross C. Hardison	The Pennsylvania State University
13-Feb-01	Marc Vidal	Harvard Medical School
15-Feb-01	Grant T. Gullberg	University of Utah
20-Feb-01	Christopher Benz	Buck Institute for Age Research
27-Feb-01	Gene Meyers	Celera Genomics
6-Mar-01	Anita B. Roberts	National Institutes of Health
15-Mar-01	Eva Y.-H.P. Lee	University of Texas Health Science Center
16-Mar-01	Thomas A. Steitz	Yale University
19-Mar-01	Ed Roos	The Netherlands Cancer Institute
20-Mar-01	Tej Pandita	College of Physicians and Surgeons, Columbia University
28-Mar-01	Jan Vijg	Cancer Therapy Research Center, Institute for Drug Development
29-Mar-01	William J. Muller	McMaster University
5-Apr-01	Catherine L. Peichel	Stanford University
10-Apr-01	Robert J. Lechleider	Uniformed Services University of the Health Sciences
17-Apr-01	Leona D. Samson	Harvard University School of Public Health
18-Apr-01	Claudia Gravekamp	San Antonio Cancer Center
1-May-01	Charles E. Samuel	University of California, Santa Barbara
8-May-01	Mary Ann Osley	University of New Mexico
15-May-01	Graham C. Walker	Massachusetts Institute of Technology
22-May-01	Michael Levine	University of California, Berkeley
23-May-01	H. Steven Wiley	Pacific Northwest National Laboratory
31-May-01	Mats Gustafsson	University of California, San Francisco
5-Jun-01	Martin Caffrey	The Ohio State University
12-Jun-01	Susan J. Fisher	University of California, San Francisco

## 2001 (cont.)

AUG 29	Nora Volkow	Brookhaven National Laboratory
SEPT 18	Barbara Meyer	University of California, Berkeley
	Helen Hobbs	University of Texas Southwestern Medical Center
25	Anat Biegon	Lawrence Berkeley National Laboratory
OCT 2	William Jagust	University of California, Davis, Medical Center
9	Mina Bissell	Lawrence Berkeley National Laboratory
16	John Reinitz	
23	Gordon Hager	National Institutes of Health
30	Edward Rubin	Lawrence Berkeley National Laboratory
NOV 6	Gary Karpen	The Salk Institute
13	John Gerdes	Central Washington University
27	Christi Walter	University of Texas Health Science Center
DEC 4	Martin Kreitman	University of Chicago
11	James Haber	Brandeis University

## 2002

JAN 1		
8	Beverly Emerson	The Salk Institute
15	David Haussler	University of California, Santa Cruz
22	James Shull	University of Nebraska Medical Center
29	Steve Kowalczykowski	University of California, Davis
FEB 5	Mark Groudine	Fred Hutchinson Cancer Center
12	Saraswati Sukumar	The Johns Hopkins University School of Medicine
19	Carl Anderson	Brookhaven National Laboratory
26	Eric Wright	University of Dundee
MAR 5	Marit Nilson-Hamilton	Iowa State University
12	Bridget Carragher	University of Illinois, Urbana-Champaign
19	Steve Elledge	Baylor College of Medicine
26	Vicki Lundblad	Baylor College of Medicine
APR 2	Peter St. George-Hyslop	University of Toronto
9	Steven Larson	Memorial Sloan-Kettering Cancer Center
16	Joan Fox	Cleveland Clinic Foundation
23	Tracy Handel	University of California, Berkeley
30	Svante Paabo	Max-Planck-Institute of Evolutionary Anthropology
MAY 7	Sanjiv Gambhir	University of California, Los Angeles
14	Steve Baylin	The Johns Hopkins University School of Medicine
21	Bing Jap	Lawrence Berkeley National Laboratory
28	Priscilla Cooper	Lawrence Berkeley National Laboratory
JUN 4	David Hovda	University of California, Los Angeles
11	Joseph DeRisi	University of California, San Francisco